

NOTES

Life-Threatening Scrub Typhus in a Traveler Returning from Thailand

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Scrub typhus is not one of the more commonly encountered diseases in travelers returning from Asia, but it deserves more consideration in view of its severity and the availability of specific chemotherapy and chemoprophylaxis. We describe a case of scrub typhus that was associated with coma and multiorgan failure in a traveler returning to the United States from Thailand. The diagnosis was made only retrospectively despite a travel history and clinical signs that suggested infection with *Rickettsia tsutsugamushi*. No specific therapy was given, and marked neurological impairment persisted 6 months after the beginning of the illness. An increased awareness of scrub typhus is a prerequisite for recommending prophylaxis and instituting prompt therapy.

Case Report

A 51-year-old male was hospitalized with pyrexia (temperature to 105°F), shaking chills, headaches, a diffuse rash, and diarrhea. On admission, a small crusted lesion with central necrosis that was described as a pustule was noted in the left scapular region. The patient had walked through rugged, hilly country in northern Thailand (near the Burmese border) from the 8th to the 12th day before the onset of symptoms and was hospitalized within a week of returning to North America. His illness progressed rapidly and was complicated by multiorgan failure. He developed adult respiratory distress syndrome that required prolonged ventilation and tracheostomy, renal failure that required dialysis, meningoencephalitis with extended coma, bilaterally decreased vision and hearing, hyperbilirubinemia (bilirubin levels reached 308 $\mu\text{mol/L}$), malnutrition, and profound weakness. The etiology of his illness could not be determined during hospitalization despite an extensive diagnostic workup that included serological testing for tropical infections such as dengue and Japanese B encephalitis. He did not receive antibiotics active against *Rickettsia tsutsugamushi*.

The diagnosis of scrub typhus was made in retrospect by assaying antibodies to *R. tsutsugamushi* with use of the highly specific indirect immunoperoxidase test [1]. Analysis

of sera obtained 2 weeks after the onset of illness revealed IgG and IgM antibody titers to *R. tsutsugamushi* of 1:800 and 1:3,200, respectively. Six months later the IgG titer had risen to 1:12,800 and the IgM titer had decreased to 1:800. By this time the patient was no longer comatose, and his condition had stabilized. However, he still had partial blindness, nerve deafness, a cognitive defect, and gait ataxia.

Discussion

The potential severity of scrub typhus, which, in this case, was acquired by a traveler to Southeast Asia, is clearly illustrated in this report. During the preantibiotic era, case-fatality rates of up to 50% were reported from Japan [2], and mortality rates remain high in some areas in which scrub typhus is endemic. We are currently investigating scrub typhus in northern Thailand, where this traveler apparently acquired his infection. The case-fatality rate in northern Thailand is 15%, and multiple-organ involvement is common. As was the case for this traveler, manifestations of disease reportedly may persist for months after *R. tsutsugamushi* infection. Neuropsychiatric abnormalities and deafness occur with particular frequency [3], and they occurred in our case.

Reports of North American tourists who acquired scrub typhus are rare; only three cases were confirmed at the Centers for Disease Control and Prevention from 1983 to 1987 [4]. There are also reports of travelers from Germany [5], New Zealand [6], and France [7] who acquired scrub typhus during trips to Thailand. *R. tsutsugamushi* infection is associated with rural habitats not usually considered to be popular with the casual traveler. Exposure occurs when individuals who camp, raft, or trek come into contact with larval mites, known as chiggers, that transmit the pathogen in their bite. Not only are such activities becoming increasingly popular with travelers but also Southeast Asia is becoming increas-

Received 1 June 1993; revised 2 August 1993.

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ingly popular as a tourist destination. More than 5 million tourists visited Thailand in 1990. It is therefore probable that physicians in the West will see increased numbers of travelers returning with scrub typhus.

The area in which scrub typhus is endemic forms a triangle bounded by northern Japan and southeastern Siberia to the north, Queensland, Australia, to the south, and Pakistan to the west. Larval mites inhabit circumscribed areas within scrub forests, tall grass, or plantations. Large numbers of cases of scrub typhus can occur when humans enter these so-called mite islands. During the Second World War, there were 18,000 cases of scrub typhus in Allied soldiers [8], and 1,255 individuals became ill with *R. tsutsugamushi* infection on two small islands off the coast of Dutch New Guinea during only a 4-month period [9].

Prompt treatment with doxycycline or chloramphenicol is the key to reducing mortality due to scrub typhus and speeding convalescence [3]. Thus, physicians must have a high index of suspicion for scrub typhus in febrile patients who have returned from an area of endemicity. Unfortunately, the diagnosis of scrub typhus can be serologically confirmed only in specialized reference centers, and no commercially available rapid diagnostic test is available. Treatment therefore must be presumptive, but the benefits of avoiding severe scrub typhus by early administration of antibiotics generally far outweigh the risks of a 1-week course of doxycycline.

The most useful clinical clue in the diagnosis of scrub typhus is the presence of a characteristic lesion called an eschar. This lesion forms at the site where the infecting chigger has bitten the individual and begins as a small, painless papule that develops during the 6–18 day incubation period. It enlarges, undergoes central necrosis, and crusts to form a lesion somewhat resembling that caused by a cigarette burn. The regional lymph nodes of patients with scrub typhus are enlarged and tender. However, as this case tragically illustrates, even a typical eschar can be overlooked or misdiagnosed. The absence of an eschar in no way rules out the diagnosis of scrub typhus because these lesions occur in only about 60% of primary infections and in considerably fewer secondary infections.

Scrub typhus produces disseminated multiorgan vasculitis and perivasculitis of the small blood vessels, a fact that helps explain the great diversity of clinical manifestations that can be encountered. In cases of scrub typhus, fever and headache begin abruptly and are frequently accompanied by myalgias, malaise, and weakness. More specific clues to the presence of scrub typhus include deafness and tinnitus, which occur in up to one-third of cases, as well as conjunctival suffusion and lymphadenopathy, which are common. A macular rash is also a sign of disease but is difficult to see on dark-skinned individuals. The rash appears on the trunk late in the first week of illness and then spreads peripherally and becomes maculopapular. Patients with mild cases of scrub typhus fre-

quently have pulmonary involvement. Respiratory distress and encephalitis are the principal causes of death in patients with severe disease.

Weekly doses of 200 mg of doxycycline can prevent *R. tsutsugamushi* infection [10, 11]. Nonimmune populations occupationally exposed would benefit most from scrub typhus protection, but chemoprophylaxis should also be considered for travelers at high risk for disease, such as those who backpack or trek in areas of endemicity. Therapy with daily doxycycline is often recommended for the prevention of falciparum malaria due to drug-resistant strains of *Plasmodium falciparum* organisms, which are particularly prevalent in parts of Asia [12], but it is not known whether this regimen will prevent scrub typhus. (Doxycycline is bacteriostatic and acts in concert with the immune response to eradicate rickettsiae. Therapy with daily doxycycline theoretically could inhibit the development of an antirickettsial immune response. Organisms that have been restrained but not killed might therefore be free to multiply when therapy with daily doxycycline was stopped. In contrast, the interval between weekly doses of doxycycline permits some organisms to multiply and a partial immune response to develop.) Contact with chiggers can be reduced by not sitting or lying directly on the ground and by applying repellent to the tops of boots and socks and to the hem of trousers.

Many travel health guides do not mention *R. tsutsugamushi* infection [13] and, even in guides that do, the availability of chemoprophylaxis is not always discussed [14]. Increased awareness of scrub typhus is necessary so that appropriate recommendations for prevention can be given to individuals who are traveling to areas of endemicity and so that early treatment can be offered to those who return with the infection.

Acknowledgments

The authors thank Ms. Panita Tanskul and Ms. Aree Futrakul for performing the indirect immunoperoxidase test.

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